**Patent**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| **CLAIMS** | Title: METHOD FOR HIGH-THROUGHPUT SCREENING ASSAY SAMPLE PREPARATION AND ANALYSIS | |
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**LISTING OF CLAIMS:**

1. (Currently Amended) A method for high-throughput screening assay sample preparation and testing for identification of binding between target compounds and library compounds, for use with a device measuring the enthalpy of reaction for such binding, comprising:

introducing not less than one selected library compound solution to a first solvent solution on the device such that they mix to form not less than one library compound/solvent solution;

introducing not less than one target compound/second solvent solution on the device;

establishing thermal equilibrium of the device;

merging said not less than one library compound/solvent solution with said target compound/solvent solution at not less than one first location on the device;

merging said not less than one library compound/solvent solution with a third solvent solution at not less than one second location on the device;

detecting a first heat of reaction for said merged library compound/solvent solution and said target compound/solvent solution;

detecting a second heat of reaction for said merged library compound/solvent solution with said third solvent solution; ~~and~~

comparing said first and second heats of reaction; and

detecting a binding operation has occurred between said merged library compound/solvent solution and said target compound/solvent solution, when the comparing step finds the first heat of reaction is greater than the second heat of reaction.

2. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 1, wherein said first solvent, said second solvent and said third solvent solutions are at approximately the same co-solvent concentration.

3. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 1, wherein said second solvent solution and said third solvent solution are at a second concentration and said first solvent solution is at a first concentration.

4. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 1, wherein said selected library compound is concentrated within a solution, said concentration having a range, wherein said range is approximately 100 micromolar to 10 millimolar concentration.

5. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 1, wherein said first solvent solution comprises an unmodified solvent solution.

6. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 1, wherein said second solvent solution and said third solvent solution comprise a modified solvent solution.

7. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 1, wherein said library compound comprises

a dried library compound material.

8. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 7, wherein said dried library compound is dissolved in a solvent solution prior to merging with said target compound/solvent solution.

9. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 1, wherein merging comprises application of electrostatic force.

10. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 1, wherein said not less than one target compound comprises dried target compound material.

11. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 4, wherein said library compound solution includes one or more co-solvents, wherein said co-solvent is present in a concentration ranging from approximately 0.1% to approximately 100%.

12. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 11, wherein said co-solvent present in said library compound solution comprises dimethyl sulfoxide, and wherein said dimethyl sulfoxide is present in a concentration ranging from approximately 50% to approximately 100%.

13. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 7, wherein said library compound/solvent material is dried at ambient temperature in a laminar flow of filtered air.

14. (Original) The method for high-throughput screening assay sample

preparation and testing according to claim 1, wherein said first solvent solution further includes target compounds.

15. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 1, wherein said target compound and second solvent are introduced separately on the device and mix on the surface of the device to form said target compound/solvent solution.

16. (Original) The method for high-throughput screening assay sample preparation and testing according to claim 1, wherein the calorimetric device is a nanocalorimetric device.

17. (Original) The method for high-throughput screening as-say sample preparation and testing according to claim 1, wherein merging comprises application of electrical force.

18. (Currently Amended) A method for high-throughput screening assay sample preparation and analysis for identification of binding between target compounds and library compounds for use within a nanocalorimeter, wherein said nanocalorimeter includes thermal isolation regions, reference regions, and measurement regions, the method comprising:

depositing not less than one drop of a first solvent solution within each of not less than one reference region and not less than one measurement region;

depositing not less than one drop of a second solvent solution within each of not less than one measurement region and not less than one reference region;

depositing not less than one drop of target compound within the measurement region, such that said not less than one drop of target compound contacts and mixes with said not less than one drop of second solvent solution to form a target compound/solvent solution;

depositing not less than one drop of selected library compound solution in the not less than one measurement region and the not less than one reference region,

such that said not less than one drop of selected library compound contacts and mixes with said not less than one drop of first solvent solution to form a library compound/solvent solution;

establishing thermal equilibrium of the not less than one measurement region and the not less than one reference region;

merging said library compound/solvent solution with said second solvent solution within the not less than one reference region;

merging said library compound/solvent solution with said target compound/solvent solution within the not less than one measurement region;

detecting a first heat of reaction for said merged library compound/solvent solution and said target compound/solvent solution within the not less than one measurement region;

detecting a second heat of reaction for said merged library compound/solvent solution and said second solvent solution within the not less than one reference region; ~~and~~

comparing said heats of reaction for the not less than one reference region and the not less than one measurement region; and

detecting a binding operation has occurred between said merged library compound/solvent solution and said target compound/solvent solution, when the comparing step finds the first heat of reaction is greater than the second heat of reaction.

19. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 18, wherein said deposited drops have a size, said size ranging from approximately 10 nL to in excess of 10 µL.

20. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 18, wherein said deposited drops have a size, said size ranging from approximately 200 nL to approximately 400 nL.

21. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 18, wherein said second solvent comprises a modified solvent.

22. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 18, further comprising depositing two drops of said solvent within said reference region.

23. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 18, wherein said library compound is in a dried form.

24. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 23, wherein mixing said test compound comprises dissolving said dried library compound within said first solvent.

25. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 18, wherein said first solvent and said second solvent are at approximately the same solvent concentrations.

26. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 18, wherein said first solvent solution and said second solvent solution are at differing solvent concentrations.

27. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 18, wherein said second solvent solution is a modified solvent solution and said first solvent solution is an unmodified solvent solution.

28. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 18, wherein merging comprises application of electrostatic force.

29. (Previously Presented) The method for high-throughput screening assay sample preparation according to claim 18, further comprising mixing said target compound and said second solvent mixed prior to deposition on the device.

30. (Currently Amended) A method for high-throughput screening assay sample preparation and analysis for use within a nanocalorimeter, wherein said nanocalorimeter includes thermal isolation regions and measurement regions, the method comprising:

depositing not less than one drop of target material within the measurement region;

depositing not less than one drop of selected library compound solution in the not less than one measurement region;

establishing thermal equilibrium within the regions of the nanocalorimeter;

merging said library compound solution with said target material solution within the not less than one measurement region;

detecting a heat of reaction for said merged library compound solution and said target material solution within the not less than one measurement region when said detecting of the heat of reaction extends for a period of time longer than a time of merging transients; ~~and~~

measuring said heat of reaction for the not less than one measurement region; and

determining a binding operation has occurred when the heat of reaction is has been detected and measured.

31. (Currently Amended) A method for high-throughput screening assay sample preparation and analysis for identification of binding between target compounds and library compounds for use with a device measuring the enthalpy of reaction for such

binding, the device having thermal isolation regions, reference regions, and measurement regions, the method comprising:

depositing not less than one drop of a first solvent solution within each of not less than one reference region and not less than one measurement region;

depositing not less than one drop of a second solvent solution within each of not less than one measurement region and not less than one reference region;

depositing not less than one drop of target compound within the measurement region, such that said not less than one drop of target compound contacts and mixes with said not less than one drop of second solvent solution to form a target compound/solvent solution;

depositing not less than one drop of selected library compound solution in the not less than one measurement region and the not less than one reference region, such that said not less than one drop of selected library compound contacts and mixes with said not less than one drop of first solvent solution to form a library compound/solvent solution;

establishing thermal equilibrium of the not less than one measurement region and the not less than one reference region;

merging said library compound/solvent solution with said second solvent solution within the not less than one reference region;

merging said library compound/solvent solution with said target compound/solvent solution within the not less than one measurement region;

detecting a first heat of reaction for said merged library compound/solvent solution and said target compound/solvent solution within the not less than one measurement region;

detecting a second heat of reaction for said merged library compound/solvent solution and said second solvent solution within the not less than one reference region; ~~and~~

comparing said heats of reaction for the not less than one reference region and the not less than one measurement region; and

detecting a binding operation has occurred between said merged library compound/solvent solution and said target compound/solvent solution, when the

comparing step finds the first heat of reaction is greater than the second heat of reaction.

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